



UWE SCHONROCK ET AL
USSN 09 132,799

ADDITIONAL FEE

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REMARKS

Background

The outstanding issues remaining for claims 1, 3, 4, 6, 11 and 12 are the six rejections made under 103(a) which are as follows:

- (1) Claims 1 and 3 - Kohmura et al.
- (2) Claims 1 and 3 - Kohmura et al. in view of Atlas of Protein Sequence and Structure
- (3) Claims 1, 3 and 4 - Kohmura et al. in view of Bundgaard and Sumner-Smith
- (4) Claims 1 and 3 - Steffens et al. in view of "Remington Pharmaceutical Sciences" and WPIDS abstract 1978-34432 (JP 53034915)
- (5) Claims 1 and 3 - Steffens et al. in view of Atlas of Protein Sequence and Structure
- (6) Claims 1, 6, 11 and 12 - Kohmura et al. or Steffens et al.

Before addressing the six rejections, it is noted that MPEP 706.02 (CHOICE OF PRIOR ART; BEST AVAILABLE) states:

"Prior art rejections should ordinarily be confined strictly to the best available art. Exceptions may properly be made, for example, where:

- (A) the propriety of a 35 U.S.C. 102 or 103 rejection depends on a particular interpretation of a claim;
- (B) a claim is met only in terms by a reference which does not disclose the inventive concepts involved; or
- (C) the most pertinent reference seems likely to be antedated by a 37 CFR 1.131 affidavit or declaration.

Such rejections should be backed up by the best other art rejection available. Merely cumulative rejections, i.e. those which would clearly fall if the primary rejection were not sustained should be avoided."

Since all of the rejections of record are 103 rejections, exception (A) does not apply. In addition, each of the references cited were cited in a previous office action whereupon the applicants did not supply a 1.131 affidavit or declaration in their response; when also viewed in light of the applicants earliest effective filing date, it would not "seem likely" to an examiner that the references would be antedated. Therefore, exception (C) does not apply.

If the need for multiple rejections stems from exception (B), this would appear to undermine the examiner's rejection based on a *prima facie* showing of obviousness.

In any event, it is requested that if the examiner maintains his rejections, that the examiner narrow the number of rejections to the use of what he believes to be his best available prior art in order to simplify the issues for Appeal.

35 U.S.C. § 103(a) rejections

Applicants respectfully request reconsideration and allowance of this application in view of the following comments.

(1) Rejection of claim 1 and 3 over Kohmura et al.

Although there are several differences with regard to the scope of the peptide sequence, the examiner states that Kohmura et al. does not teach administration of the peptides in the form of a pharmaceutical composition which is not exactly correct as the claims read upon "cosmetic or dermatological topical water-in-oil preparations."

The deficiencies of Kohmura et al. are explained away by stating that it would be obvious to prepare a pharmaceutical composition with a compound with known activity (i.e. inhibition of ACE-activity). ***The applicants request reconsideration of this position based on two observations:***

First, preparation of a pharmaceutical composition with a VVRP peptide sequence for the purpose of inhibiting ACE-activity entail the formulation of an oral or parenteral composition not a topical one (see Exhibit 1 - pages 743-745 of *Goodman and Gilman's The Pharmacological Basis of Therapeutics* for discussion of history and pharmacokinetics of ACE-inhibitor compounds) as the former drug delivery methods are necessary to obtain an adequate blood serum concentration of the ACE-inhibitor to produce the desired effects.

In addition, it is well known that ***one of the side effects of ACE-inhibitors is skin rash*** (see page 751, col. 1, *ibid.*) and as such one of ordinary skill in the art would not be directed toward formulating ***cosmetic or dermatological topical*** compositions with ACE-inhibitor compounds, Kohmura et al. "teaches away" from the applicants formulation. (The examiner cites U.S. 5,346,887 but does not make it part of the rejection; however, even if it was included, it is noted that '887 recites ***topical ocular*** administration not ***topical dermatological***).

Second, the examiner explains that it is well known to form pharmaceutical compositions from active compounds ("Anyone would be capable of preparing a composition from a known compound). However, the motivation for doing so appears to come from the examiner himself

rather than from a teaching or suggestion from the prior art. MPEP 2143.01 states that "Fact that references can be combined or modified is not sufficient to establish *prima facie* obviousness" and "Fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness."

The examiner also cites *In re Rosicky* to buttress his position. However, MPEP 2143.03 states that "Legal precedent can provide the rationale supporting obviousness only if the facts in the case are sufficiently similar to those in the application." *Rosicky* (which dealt with xanthene derivatives) would apply only for circumstances where the intended use of the compositions are the same. *In re Anthony*, 162 USPQ 595, (CCPA 1969) cited how the findings in *Rosicky* should be interpreted narrowly not broadly:

"The board's reliance on *In re Rosicky*, 47 CCPA 859, 276 F.2d 656, 125 USPQ 341 (1960), in support of its position is misplaced, appellant says, because there composition claims similar in form to those here were held unpatentable over a group of prior art compounds, including the active ingredients of the claims, which in contrast to the present case, were disclosed to have the *very same specific pharmaceutical utility* as did the active compounds of the claimed compositions. *It was in those circumstances* the court held that the mere formulation of pharmaceutical compositions containing certain amounts of the active ingredients of the prior art and a pharmaceutical carrier would be obvious to one of ordinary skill in the art. *We agree with the appellant.*"

Lastly, it is well known that MPEP 2143.03 states that "To establish *prima facie* obviousness of a claimed invention, ***all the claim limitations must be taught or suggested by the prior art.*** *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)." The fact that claims 1 and 3 were also rejected over Kohmura et al. in view of Atlas of Protein Sequence and Structure (and also separately Kohmura et al. in view of Bungaard and Sumner-Smith) would seem to be *prima facie* evidence that Kohmura et al. does not teach or suggest all the claim limitations.

For these reasons, it is believed that claims 1 and 3 are non-obvious in view of the Kohmura et al. reference.

(2) Rejection of claims 1 and 3 over Kohmura et al. in view of Atlas of Protein Sequence and Structure

Atlas of Protein Sequence and Structure (referred to as Atlas for this paragraph) is combined with Kohmura et al. However, Atlas appears to be used less to remedy the lack of a teaching of a composition/preparation form and a form for a specific purpose for the peptides disclosed in Kohmura et al. and more to fill in the gaps for the scope of peptides claimed to be used by the applicants which are not disclosed in the Kohmura et al. reference.

As such, the arguments made above against Kohmura et al. would also apply here. It is also presented that there is no teaching or suggestion within Kohmura et al. or Atlas which provides the motivation for the substitution or addition of the peptides disclosed by Atlas into the teachings of Kohmura et al. to arrive at the applicants' preparation (see MPEP 2143.01).

Lastly, the fact that claims 1 and 3 were also rejected over Kohmura et al. in view of Bungaard and Sumner-Smith would seem to be *prima facie* evidence that Kohmura et al. does not teach or suggest all the claim limitations (see MPEP 2143.03).

For these reasons, it is believed that claims 1 and 3 are non-obvious over Kohmura et al. in view of Atlas.

(3) Rejection of claim 1, 3 and 4 over Kohmura et al. in view of Bungaard and Sumner-Smith

Bungaard and Sumner-Smith is combined with Kohmura et al. However, these references appear to be used less to remedy the lack of a teaching of a composition/preparation form and a form for a specific purpose for the peptides disclosed in Kohmura et al. and more to fill in the gaps for the scope of peptides claimed to be used by the applicants which are not disclosed in the Kohmura et al. reference.

As such, the arguments made above against Kohmura et al. would also apply here. It is also presented that there is no teaching or suggestion within Kohmura et al., Bungaard or Sumner-Smith which provides the motivation for the substitution or addition of the peptides disclosed by Atlas into the teachings of Kohmura et al. to arrive at the applicants' preparation (see MPEP 2143.01).

Lastly, the fact that claims 1 and 3 were also rejected over Kohmura et al. in view of Atlas Protein Sequence and Structure would seem to be *prima facie* evidence that Kohmura et al. does not teach or suggest all the claim limitations (see MPEP 2143.03).

For these reasons, it is believed that claims 1, 3 and 4 are non-obvious over Kohmura et al. in view of Bungaard and Sumner-Smith.

(4) Rejection of claims 1 and 3 over Steffens et al. in view of Remington Pharmaceutical Sciences and WPIDS abstract 1978-34432 (JP 53034915)

The examiner presents that Steffens et al. teaches VVRP proteins used as *pharmaceutical compositions* with improved fibrinolytic characteristics and thrombolytic activity and that the difference between the Steffens et al. reference and the applicants claimed invention resides in the "water-in-oil" limitation. However, this is only partially correct as the difference is that

Steffens et al. teaches a pharmaceutical composition whereas the applicants are claiming a cosmetic or dermatological topical water-in-oil preparation.

Again, because of the nature of the compositions and their intended activity, Steffens et al. teaches a composition which is not intended for topical administration but administration of a bolus (see claim 19 and col. 12, line 59 - col. 14, line 39).

Neither Remington Pharmaceutical Sciences nor the abstract for JP 53034915 provide the requisite motivation to modify the pharmaceutical compositions taught by Steffens et al. to arrive at the cosmetic or dermatological topical preparations claimed by the applicants. Moreover, any effort to convert the compositions of Steffens et al. into topical formulations would cause the formulation to be unusable for the intended purpose disclosed by Steffens et al. (i.e. as a composition with improved fibrinolytic properties and thrombin activity). MPEP 2143.01 states that "If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)."

Lastly, the fact that claims 1 and 3 were also rejected over Kohmura et al. in view of Atlas of Protein Sequence and Structure would seem to be *prima facie* evidence that Kohmura et al. does not teach or suggest all the claim limitations (see MPEP 2143.03).

For these reasons, it is believed that claims 1 and 3 are non-obvious over Steffens et al. in view of Remington Pharmaceutical Sciences and the abstract for JP 53034915.

(5) Rejection of claims 1 and 3 over Steffens et al. in view of Atlas of Protein Sequence and Structure

Atlas of Protein Sequence and Structure (referred to as Atlas for this paragraph) is combined with Steffens et al. However, Atlas appears to be used less to remedy the lack of a teaching of a composition/preparation form and a form for a specific purpose for the peptides disclosed in Steffens et al. and more to fill in the gaps for the scope of peptides claimed to be used by the applicants which are not disclosed in the Steffens et al. reference.

As such, the arguments made above against Steffens et al. would also apply here. It is also presented that there is no teaching or suggestion within Steffens et al. or Atlas which provides the motivation for the substitution or addition of the peptides disclosed by Atlas into the teachings of Steffens et al. to arrive at the applicants' preparation (see MPEP 2143.01).

Lastly, the combination of Steffens et al. in view of Atlas does not teach or suggest all the claim limitations, especially with regard to the scope of peptides used (see MPEP 2143.03).

For these reasons, it is believed that claims 1 and 3 are non-obvious over Steffens et al. in view of Atlas.

(6) Rejection of claims 1, 6, 11 and 12 over Kohmura et al. or Steffens et al.

Claims 11 and 12 are dependent upon claim 6 which in turn is dependent upon claim 1. The comments presented above establish that Kohmura et al. and Steffens et al. do not render preparation of claim 1 to *prima facie* obvious and as such the concentration ranges cited in claims 6, 11 and 12 for these claimed preparations would also be non-obvious. (Note: Steffens et al. was never used alone to reject any of the claims prior to this rejection) Even if *in arguendo*, it was held that Kohmura et al. and Steffens et al. rendered preparation *prima facie* obvious, the intended use of the formulations as described by Kohmura et al. and Steffens et al. would require higher concentration levels of peptides than those currently claimed.

For these reasons, it is believed that claims 1, 6, 11 and 12 are non-obvious over Kohmura et al. or Steffens et al.

Closing

Applicants believe that this application is in condition for allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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HCL:ja

Attachment: **Exhibit 1** - Pages 743-751 from Goodman and Gilman's The Pharmacological Basis of Therapeutics

CERTIFICATE OF MAILING

I hereby certify that the foregoing Amendment Under 37 CFR 1.111 is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Hon. Commissioner of Patents, Washington, D.C. 20231, on the date indicated below:

Date: **27 July 2001**

By Howard C Lee
Howard C. Lee